REVIEW

Metabolic characteristics and health effects of low-calorie sweeteners focusing on the prevention of obesity and metabolic diseases

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Summary
Low-calorie sweeteners (LCSs) are attracting attention as sugar substitutes, and many studies are being conducted, especially in relation to the prevention of obesity and metabolic diseases. These sweeteners are characterised by low calories and blood sugar index (*GI*), and may play a role in minimising insulin response and suppressing weight gain. In this review paper, the chemical structure and metabolic characteristics of representative LCSs (allulose, erythritol, stevia, etc.) were analysed, and their effects on health were comprehensively considered. In particular, the efficacy and limitations of LCSs were compared, focusing on their association with obesity, type 2 diabetes and cardiovascular disease. In addition, the recently researched physiological mechanisms of sweeteners and their interactions with microbiomes were discussed. Finally, by evaluating the regulatory status and industrial application potential of each country, the directions for continuous research and application of LCSs were presented. The purpose of this study is to provide a scientific basis for healthy sweetener choices for the prevention of metabolic diseases.

Keywords
low-calorie sweeteners; allulose; metabolic health; obesity; blood sugar control

Sugar has been called the “white devil” and has been accused of increasing the risk of diabetes, obesity, and cardiovascular disease [1]. Sweetness is a characteristic of food and beverages that humans perceive through taste receptors from infancy. Structurally, a variety of compounds are perceived as sweet. Low-calorie sweeteners (LCSs) and non-calorie sweeteners (LNCSs) have replaced carbohydrate sweeteners for more than a century as a means of reducing energy (calorie) intake and controlling blood sugar levels in diabetics [2, 3].

Sugar-free or low-sugar foods and beverages are very popular in the United States and other countries, and the sweeteners that make this possible are some of the most recognisable ingredients in the food supply [4]. LCSs provide palatable alternatives to calorie sugars such as saccharose and high-fructose corn syrup and are commonly found in soft drinks, sweetener packets, grains, snack foods, dairy products, sanitation products, and pharmaceuticals [5]. The effects of these sugar substitutes have not been well studied, and their short- and long-term effects have yet to be determined [6]. In recent years, LCSs consumption seems to have increased among people of all ages. It is estimated that 28 % of the global population consumes LCSs. This is partly due to the growth of the packaged food market, which is referred to as ‘diet’ food and beverage [7]. Most LCSs consumers have been reported to consume once a day (80 % of children and 56 % of adults), and in adults, the frequency of intake has increased with weight. In adults, women had higher LCSs intake than men, and in obese individuals, they had higher LCSs intake than overweight and normal-weight individuals.

To elucidate the effects of LCSs on weight, several potential mechanisms have been proposed, including the promotion of appetite and energy intake due to LCSs [8]. Existing evidence suggests that LCSs may be a useful tool for those who actively manage their weight for weight loss and maintenance [9]. It is estimated that reduc-

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ing their intake by 100 kcal (418.4 kJ) per day may prevent weight gain in adults. Changing regular soda to diet soda can save you around 150 kcal (627.6 kJ), and using LCSs instead of consuming 2 teaspoons (cca 18 g) of sugar in a cup of coffee three times per day will save you around 100 kcal (418.4 kJ) [10].

From a public health perspective, we are particularly concerned because overweight and obesity are associated with an increased risk of various chronic and debilitating diseases, including cancer, cardiovascular disease, and diabetes [11]. Obesity is an urgent public health issue in the United States and globally. As obesity and its consequent complications have become unprecedentedly common, emphasis has been placed on reducing calorie intake and especially reducing added sugar [12].

LCSs are used worldwide to enhance the flavour of foods and beverages without the presence of calories from sugar. However, it has recently been argued that LCSs promote obesity [13]. While LCSs found in food supply is a regulated food additive generally recognised as safe (GRAS) by the US Food and Drug Administration (FDA, Silver Springs, Maryland, USA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA, Food and Agriculture Organization, Rome, Italy and World Health Organization, Geneva, Switzerland), and European Food Safety Agency (EFSA, Parma, Italy), the use of LCSs in food supply is controversial, especially with respect to the effect of LCSs on weight [14].

As a potential means of slowing down the obesity epidemic, LCSs are attracting attention as a dietary tool to help comply with weight loss plans or prevent excessive weight gain [15]. This knowledge is critical because the presence of LCSs in the food supply chain is high and expanding, and rodent data have suggested that their use increases energy intake, increases weight, and increases body obesity [16]. Although the relationship between obesity and energy intake is complex, a basic principle remains that an energy imbalance where energy intake exceeds energy expenditure leads to weight gain [17]. As obesity continues to rise worldwide, LCSs have become a popular sugar replacement, especially in ‘diet’ and ‘light’ foods, allowing different products to maintain their flavour without related calories, forming a perception that they are ‘healthier’ products [18]. Moderate consumption of artificial sweeteners in place of sugar can be a useful strategy for managing weight [19].

Accordingly, this review aims to examine the metabolic characteristics and health effects of LCSs, with a particular focus on their relevance to the prevention of obesity and metabolic diseases.

MATERIALS AND METHODS

Search strategy

This narrative review was conducted to explore the metabolic properties and health effects of low-calorie sweeteners (LCSs) with the aim of integrating the literature and critically evaluating it, with a particular focus on the prevention of obesity and metabolic diseases. Although this review was a narrative literature review, we search articles in databases PubMed, Medline (both National Library of Medicine, Bethesda, Maryland, USA), Web of Science (Clarivate, London, United Kingdom), Scopus (Elsevier, Amsterdam, Netherlands), RISS International (Korean Educational and Research Information Service, Daegu, South Korea), ResearchGate (ResearchGate, Berlin, Germany), and Google Scholar (Google, Mountain View, California, USA) in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [20]. Literature searches were conducted through extensive searches. Strategies with keywords: “low-calorie sweeteners”, “non-nutrient sweeteners”, “allulose”, “erythritol”, “stevia”, “obesity”, “glycemic control” and “metabolic health”. The literature search strategy and review process are as follows. PRISMA 2009 flow rules can be found in Fig. 1.

The PRISMA diagram illustrates the selection process for the narrative review. Records were identified from multiple databases from 2000 to 2025. After removing 120 duplicates, 620 records remained. A total of 118 records were screened by title and abstract, and 55 full-text articles were assessed for eligibility. After excluding 63 articles due to reasons such as preprint status, missing full text, or lack of raw data, 55 articles were ultimately included in the review.

Eligibility criteria

The articles included in this review had to meet the eligibility criteria as follows. Studies on the metabolic mechanisms, physiological outcomes, or regulatory aspects of LCS associated with obesity and metabolic disorders were considered. The included papers originally consisted of research, systematic review, narrative review, and short communication. Papers that did not focus on the metabolism or health outcomes of LCSs, lacked primary data, or were not accessible in the full text were excluded.

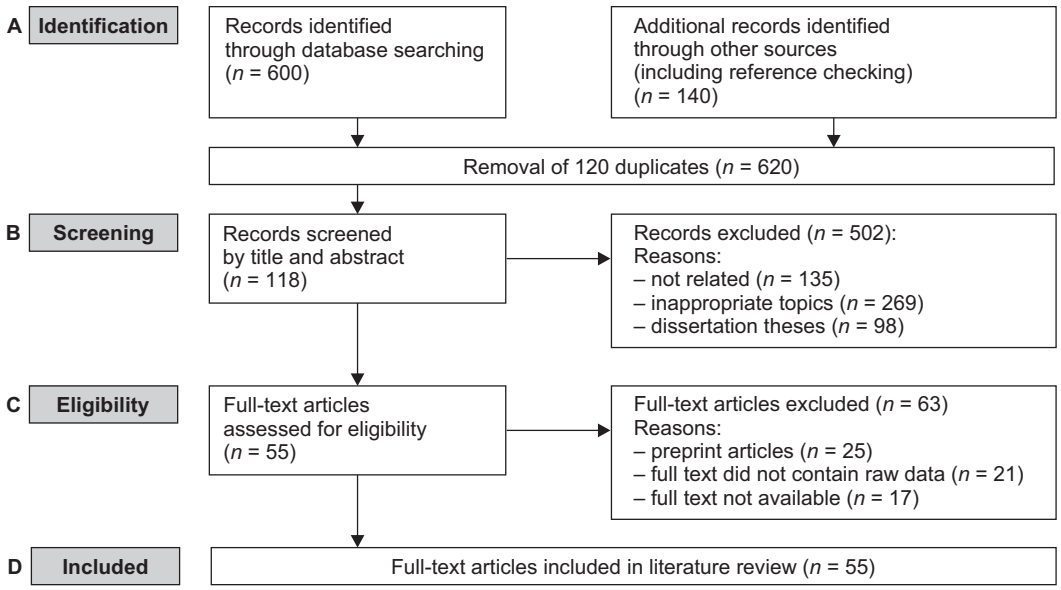

Fig. 1. PRISMA flow diagram for criteria of exclusion and inclusion.

Screening and data extraction

Consideration of various types of papers, such as original research and papers, review articles, short communication, perspective, and internet articles were included. There were no restrictions on publication dates or languages. Exclusion criteria were full text without raw data, full text without access, dissertation theses, inappropriate topics, unrelated to the main focus of this review.

Risk of bias assessment

The methodological quality of the included studies was evaluated independently by all authors.

Study selection and data extraction

Studies were identified through a manual search, and the title and abstract were reviewed and evaluated. Articles that did not match the inclusion/exclusion criteria were excluded.

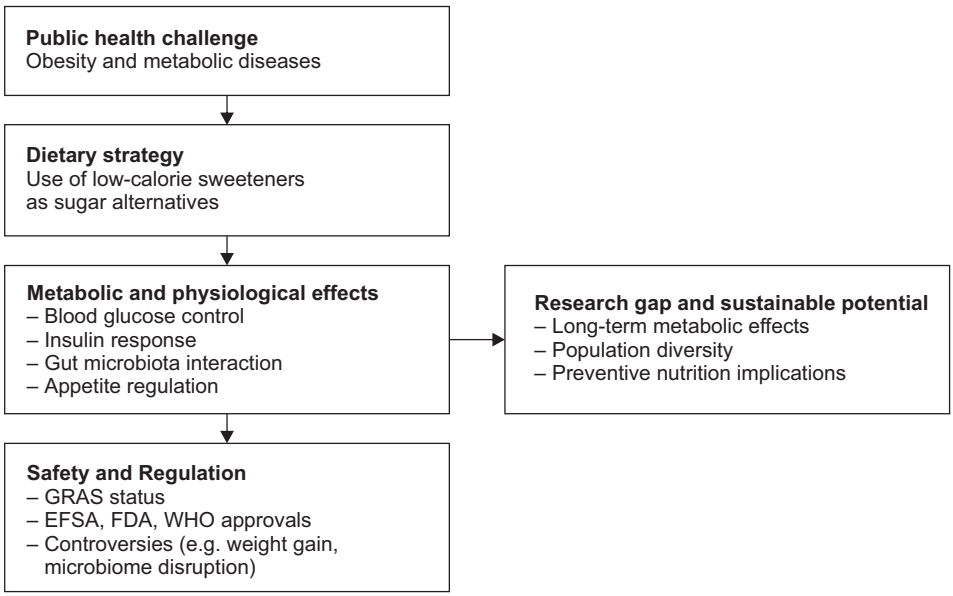

Fig. 2. Conceptual framework of the review.

In this review, professional papers were reviewed to determine whether to include the final remaining papers, excluding those that did not match the criteria. The draft results were discussed among co-authors and the final version was approved by all.

A total of 101 papers included in this review can be grouped into the following headings:
- chemical and structural properties of LCS,
- metabolic pathways and effects on blood sugar and insulin,
- LCS and intestinal microbiological interaction,
- the role of LCS in the prevention of obesity and metabolic diseases,
- status of industrial applications and regulations,
- safety and controversy.

A total of 55 papers were selected in the final stage, published between 2000 and 2025. The conceptual framework of this review and an overview of how LCSs relate to public health challenges, dietary strategies, metabolic effects, safety considerations, and future research directions is illustrated in Fig. 2.

RESULTS

Types and characteristics

LCSs can be broadly divided into two groups. Mass sweeteners (e.g. polyols) that have a sweetness similar to saccharose and are commonly used for other functional purposes in the product. Intense sweeteners, which are several times sweeter than saccharose, are mainly used only as sweeteners [21]. Each sweetener has different properties, such as sweetness intensity, metabolism, and thermostability, and is used in a variety of industries, as shown in Tab. 1.

Artificial sweeteners are manufactured by synthetic chemical methods and are characterised by their strong sweetness in very small amounts. Typical artificial sweeteners include aspartame, sucralose, saccharin, and acesulfame K [2]. Aspartame is commonly used in very-low-calorie diets and has been widely approved as a food additive with no side effects [22].

The first non-nutritive sweetener (NNS) to be commercialised was saccharin. As with many interesting findings in medical history, the compound was accidentally discovered by two chemists at Johns Hopkins Laboratory in the late 1800s [23].

Sugar-free or low-sugar foods and beverages are very popular in the United States and other countries, and the sweeteners that make this possible are among the most recognisable ingredients in the food supply [4]. While most modern sweeteners, acesulfame K, advantame, aspartame, neotame, and sucralose, have been approved in the United States through the Food Additives Process, the most recent sweetener approvals for steviol glycosides and lohan guo have been made through a GRAS system based on scientific procedures [24]. Aspartame has become an LNCS, particularly widely used in beverages. Although its metabolism is simple and well documented, the safety of aspartame remains a hot topic of attention despite its worldwide approval and recent comprehensive re-evaluation by the EFSA. The EFSA concluded that aspartame has “no safety concerns” at current consumption levels [2].

Natural sweeteners are sweet substances derived from nature, including stevia, monkey fruit, and luo han guo. Stevia is suitable for diabetes and weight control diets because it has a strong sweet taste due to steviol glycosides and does not affect blood sugar levels [25]. Monkfruit sweeteners also have antioxidant effects and are also used in functional foods [26]. Sugar alcohol is a sweetener made by chemically modifying natural sugars such as erythritol, xylitol, maltitol, sorby, etc. They are sweetened while having lower calories than sugar and are often used in gum, candy, toothpaste, because they are effective in preventing tooth decay [27]. However, some fermentation when consumed in excess [28].

Tab. 1. Comparison of low-calorie sweeteners and non-calorie sweeteners.

Sweetener	Compound classification	Sweetness intensity	Approximate amount that replaces 25 g of sugar [mg]
Acesulfame K	Oxathiazinone dioxide	≈ 200 times	125 mg
Aspartame	Methylated dipeptide	≈ 200 times	125 mg
Saccharin	Benzoic acid sulfimide	300 times	80 mg
Steviol glycosides	Glycosylated diterpenes	200–300 times	80–125 mg
Sucralose	Chlorinated disaccharide	≈ 600 times	40 mg

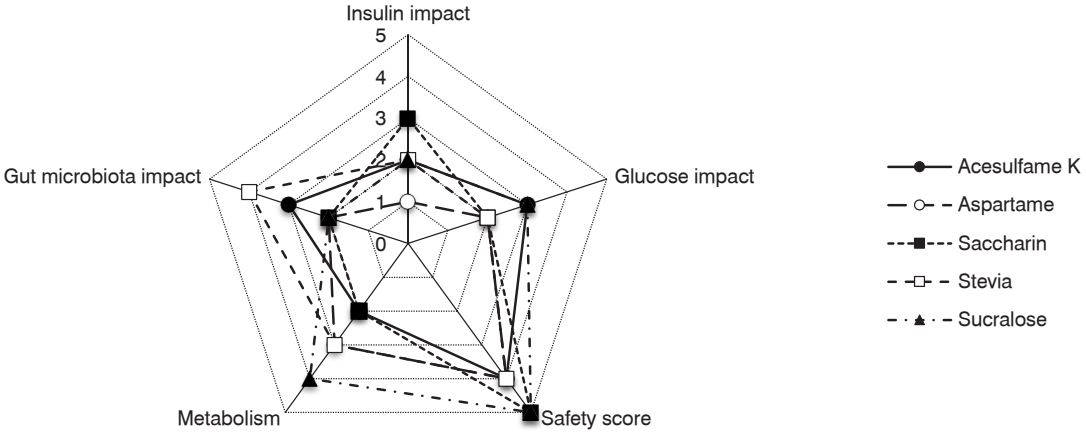

Fig. 3. Metabolic effects of low-calorie sweeteners.

Tab. 2. Metabolic effects of low-calorie sweeteners.

Sweetener	Glucose impact	Insulin impact	Gut microbiota	Metabolic pathway complexity	Safety
Acesulfame K	Low	Low	Moderate	Moderate	High
Aspartame	Low	Low	Low	High	High
Saccharin	Low	Low	Moderate	Moderate	Moderate
Steviol glycosides	None	None	Mild	Moderate	Very High
Sucralose	None	None	Disruptive	Simple	High

Metabolic effects

The metabolic effects of LCSs depend on the type of sweeteners. Artificial sweeteners are not metabolised or rarely metabolised in the body and, as a result, have little effect on blood sugar levels [29]. For example, aspartame is degraded in the small intestine, and its degradation products, aspartic acid and phenylalanine, are processed through various metabolic pathways in the body, as shown in Fig. 3. Sucralose or acesulfame K are excreted as they are without being metabolised in the body [2]. Meanwhile, some studies suggest that LCSs may affect gut microbiota. Human and animal studies have shown that LCSs may affect glucose metabolism, satiety, and vascular function despite their inherent lack of energy [6]. These studies provide important clues about the effects of LCSs on the prevention of metabolic diseases, as shown in Tab. 2. Follow-up studies are needed to further understand their metabolic characteristics [30]. The effects of intake of LCSs on blood sugar and insulin responses show different results depending on studies. Some studies have reported that LCSs do not induce elevated blood glucose and do not affect insulin secretion [29], while others point out that some sweeteners may indirectly induce insulin resistance [31]. In particular, sweeteners such as aspartame are known to minimise their effects on insulin response, but several studies still emphasise the need for multifaceted investigations [32].

The role in obesity and metabolic disease prevention

Although it is expected that the use of LCSs to replace or partially replace added sugar in

Tab. 3. Summary of clinical studies on low-calorie sweeteners and body weight.

Study	Participants	Intervention	Outcome	Notes
Peters and Beck [9]	Adults	Beverages with low-calorie sweeteners vs sugar-sweetened	Reduced weight gain	Supports substitution
Rogers et al. [24]	Adults and animals	Various low-calorie sweeteners	Mixed findings	Needs long-term follow-up
Swithers [11]	Children	Non-nutritive sweeteners intake	Potential risk	Observational data

food and beverages may reduce energy intake, it has been widely reported in recent years that consumption of LCSs may increase the risk of becoming overweight and obese [29]. A balance of evidence indicates that in children and adults, the use of LCSs instead of sugar (saccharose) may result in a reduction in energy intake and weight. Current evidence, although still limited, indicates no difference or similar effect when comparing LCSs with water [33]. Observational data suggest that NNS may promote weight gain through mechanisms such as cravings, reward phenomena, and addictive behaviour involving opioid receptors. In contrast, intervention studies show that replacing sugar-sweetened beverages with NNS (Tab. 3), leads to reduced calorie intake and moderate weight loss, as illustrated in Fig. 4 [34]. LCSs have little or no effect on blood sugar and thus may be an effective replacement for diabetes prevention [35]. In particular, natural sweeteners such as stevia do not raise blood sugar levels and thus may be safely used in diabetic patients [29]. Sugar has received significant attention due to its association with weight gain. For this reason, strategies have been developed to reduce added sugar. Non-calorie sweeteners or LCSs have been used to prevent and control weight gain [36]. Ongoing studies investigate the potential LCSs' contribution to the prevention of metabolic diseases other than obesity and diabetes. For example, some studies have reported that consumption of LCSs may have a positive effect on improving risk factors for cardiovascular disease [37].

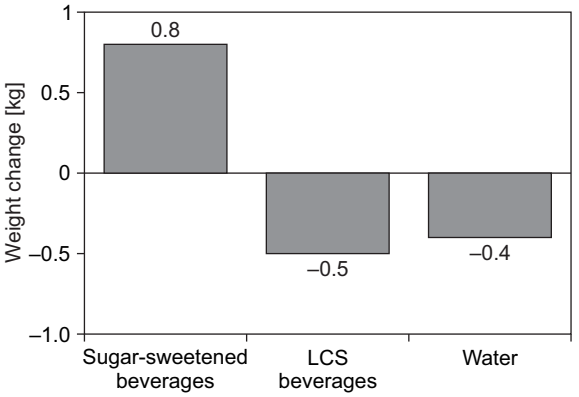

Fig. 4. Impact of beverage choice on body weight.
LCS – low-calorie sweetener.

Industrial applications and market trends

LCSs are widely used in diet soda, sports drinks, functional foods, desserts, and dairy products. In particular, the alternative sweeteners market is expanding as consumers' demand to reduce sugar consumption is increasing [38]. Approximately 30 % of US adults consumed some type of LCSs, 19.5 % consumed LCSs drinks, 11.4 % consumed desk LCSs, and 4.6 % consumed LCSs foods [39]. LCSs are used as supplements and pharmaceutical supplements for diabetics or consumers who need to control their weight. In particular, stevia and erythritol are recognised as natural sweeteners and are gaining high popularity in diabetes management foods and health-functional foods [40]. The LCSs market was valued at approximately 8.8 billion US dollars (i.e. 7.5×10^9 EUR) in 2020 and is expected to grow at an annual average of 5.1 % by 2027 [41]. With North America and Europe occupying the major markets, sweetener consumption is increasing in the Asia-Pacific region with the spread of health and well-being trends as shown in Fig. 5. In particular, the growing demand in China and India is noticeable, and competition between local brands and global companies is intensifying [42]. In addition, as government regulations are strengthened, the number of countries introducing sugar taxes has increased, further accelerating the demand for alternative sweeteners [43]. Major sweetener manufacturers include Cargill (Minneapolis, Minnesota, USA), Tate & Lyle (London, United Kingdom), Ingredion (Westchester, Illinois, USA), Roquette (Lestrem, France), Ajinomoto (Tokyo, Japan), who are introducing new sweetener technologies using research and development activities. In particular, efforts to improve blended sweetener technologies and taste profiles are prominent, and the development of bio-based sweeteners to produce sustainable sweeteners is actively underway [28]. In addition, as research continues on the health effects of alternative

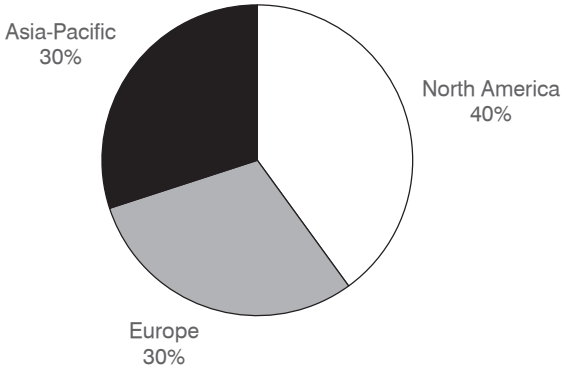

Fig. 5. Regional market share of low-calorie sweeteners.

Tab. 4. Regulatory approval and acceptable daily intake of common sweeteners.

Sweetener	FDA [2]	EFSA [30]	MFDS [44]	*ADI* [mg·kg^{-1}d^{-1}]
Acesulfame K	Approved	Approved	Approved	15
Aspartame	Approved	Approved	Approved	40
Saccharin	Approved	Approved	Approved	5
Steviol glycosides	Approved	Approved	Approved	4
Sucralose	Approved	Approved	Approved	15

FDA – Food and Drug Administration (Silver Springs, Maryland, USA), EFSA – European Food Safety Authority, Parma, Italy, MFDS – Ministry of Food and Drug Safety (Cheongju, South Korea), *ADI* – acceptable daily intake.

sweeteners, securing data on the safety and long-term effects of sweeteners within the industry has become an important issue [27].

Regulatory framework and safety considerations

Regulatory approval status and acceptable daily intake (*ADI*) of the most common sweeteners are described in Tab. 4 [2, 30, 44]. In the United States, the FDA regulates the use of sweeteners as food additives. Additionally, sweeteners classified as GRAS can be used without a separate approval process [45]. In the European Union, the EFSA is assessing the safety of sweeteners and manages a list of approved sweeteners. In Europe, an E-number is assigned to each sweetener, and the allowable usage and coverage are set [46].

As of February 2025, the FDA has approved six chemically defined food supplements for use in the USA: aspartame, acesulfame K, advantame, neotame, saccharin, sucralose. Additionally, three types of plant-derived sweeteners are generally recognised as safe (acronym GRAS): certain steviol glycosides obtained from the leaves of *Stevia rebaudiana* or fermentation-based processes, extracts from *Siraitia grosvenorii* (swingle fruit, also known as Luo Han Guo or monk fruit) and thaumatin [47].

The list of EFSA-approved sweeteners contained 21 items as of February 2025: sorbitols, mannitol, acesulfame K, aspartame, cyclamates, isomalt, saccharins, sucralose, thaumatin, neohesperidine DC, steviol glycosides from stevia, enzymatically produced steviol glycosides, glucosylated steviol glycosides, neotame, salt of aspartame-acesulfame, polyglycitol syrup, maltitols, lactitols, xylitol, erythritol, advantame. However, several of these items were subject to EFSA re-evaluation, so changes in the near future are possible [48].

The safety of LCSs is evaluated through various toxicological studies and human trials. Key safety assessment factors include acute toxicity, chronic toxicity, carcinogenicity, reproductive toxicity, and metabolic effects [49]. Aspartame is degraded in the body to phenylalanine, aspartic acid, and methanol, and some studies have raised concerns about toxicity due to methanol metabolism. However, after a comprehensive review of existing findings, the FDA and EFSA concluded that aspartame can be safely used at an approved level [50]. Sucralose has a sweetness that is about 600 times stronger than sugar and is excreted with little metabolism in the body. Although some studies have suggested the possibility of producing harmful compounds when heated at high temperatures [51], studies to date have not found any significant risk in the general level of intake [52]. Erythritol is a natural sweetener, which is known to have no elevated blood sugar and does not induce an insulin response [53]. However, recent studies have suggested that high concentrations of erythritol intake may be associated with cardiovascular disease, but further research is needed [54]. LCSs are thoroughly managed by various international regulatory agencies, and sweeteners approved to date are evaluated to be safe within established standards of use [49]. However, studies on the long-term health effects should be conducted continuously, and in particular, the effects of metabolic characteristics of certain sweeteners on individual health need to be analysed in more depth [55].

Limitations

This narrative review has several limitations. First, although a structured literature search was conducted, the selection process did not fully follow systematic review protocols, which may have introduced selection bias. Second, only English-language publications were included, potentially leading to language bias. Finally, the long-term metabolic effects of low-calorie sweeteners remain unclear due to the limited availability of long-duration human studies.

CONCLUSIONS

This review is distinct from prior studies in that it synthesises recent evidence not only on the metabolic effects of low-calorie sweeteners, but also on their potential role as preventive agents against obesity and metabolic diseases. Unlike previous reviews, this study integrates emerging findings on microbiota interactions, regulatory perspectives, and industrial trends, providing a comprehensive and updated perspective on the implications of LCSs for public health. One way to reduce sugar content is by using LCSs as substitutes. However, with the use of LCSs, questions have since been raised about the intake of these ingredients. For example, the role of LCSs in weight management is a subject of considerable controversy. LCSs have the potential to play an important role in the prevention of metabolic diseases such as obesity, diabetes, and cardiovascular diseases, as well as in the food and beverage industries as a sugar replacement. Many argue that LCSs have established themselves as a useful tool to reduce calorie intake while maintaining sweetness, especially in the prevention of obesity and metabolic diseases. Nevertheless, the long-term effects of LCSs on metabolism in the body remain controversial. This suggests that there is a lack of research to understand the exact effects of LCSs on metabolic processes. Existing studies on the metabolic properties of LCSs report that LCSs provides lower calories than sugar and has the advantage of having less effect on blood sugar levels or insulin response. These characteristics may have a positive effect on diabetics or consumers who need weight management. However, some recent studies have also suggested that LCSs may affect intestinal microbiota, resulting in changes in the metabolic process. For example, studies have shown that certain LCSs may alter the composition of intestinal microbiota and, consequently, energy metabolism. This highlights the need to take a closer look at the effects of LCSs on the body's metabolic system. Discussions about the role of LCS in the prevention of obesity and metabolic diseases have emerged as an important public health issue. LCSs reduce calorie intake and can be used as a useful tool for weight management, especially as a replacement for high-calorie foods. Studies have shown that using LCSs can reduce calorie intake by approximately 100–150 kcal (418.4–627.6 kJ) per day, which helps to prevent weight gain. However, some studies have suggested that LCSs may promote weight gain, which requires a careful approach to the use of LCSs. For example, mechanisms have been suggested that excessive use of LCSs may increase appetite or promote energy intake. This suggests a warning that although LCS can be useful as a strategy for weight loss, excessive dependence should be avoided. Further studies on the metabolic characteristics and health effects of LCSs are still needed. In particular, studies on how LCSs are metabolised in vivo and their long-term health effects are lacking. In addition, studies with diverse population groups are essential to more accurately assess the effects of LCSs on weight and metabolic diseases. Although the results of studies to date suggest that the use of LCSs may be helpful in weight management, more clinical studies and long-term observations are needed to draw clear conclusions about its effects and side effects. LCSs are widely used in many industries as sugar substitutes and have the potential to play an important role in the prevention of obesity and metabolic diseases. However, controversy continues over the metabolic effects of LCSs and its long-term health effects, which should be clarified in future studies. In conclusion, while LCSs may be an important tool for the prevention of obesity and metabolic diseases, their use requires a careful approach, and it is important to accurately understand the role of LCSs through more specific and in-depth research.

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Received 22 April 2025; 1st revised 25 May, 2025; accepted 25 June 2025; published online 2 July 2025.